UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/988,899	11/19/2001	Hendricus Renerus Jacobus Mattheus Hoogenboom	10280-139001	9170

26161 7590 03/30/2007

FISH & RICHARDSON PC
P.O. BOX 1022
MINNEAPOLIS, MN 55440-1022

EXAMINER	
LIU, SUE XU	
ART UNIT	PAPER NUMBER
1639	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/30/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	09/988,899	HOOGENBOOM, HENDRICUS RENERUS JACOBUS M	
	Examiner	Art Unit	
	Sue Liu	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 December 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,11,12,15 and 16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,11,12,15 and 16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/14/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 12/14/06 has been entered.

Claim Status

2. Claims 4-10, 13 and 14 have been cancelled.

Claims 1-3, 11, 12, 15 and 16 are currently pending.

Claims 1-3, 11, 12, 15 and 16 are being examined in this application.

Priority

3. This application is a continuation of PCT/US00/13682, filed May 18, 2000, which is claims foreign priority to an European application 99201558.6, filed May 18, 1999.

Information Disclosure Statement

4. The IDS filed on 12/14/06 has been considered. See the attached PTO-1449 form.

Claim Rejections Maintained

Claim Rejections - 35 USC § 102

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Rejection over '108 Patent

6. Claims 1-3, 11, 12, 15-16 are rejected under 35 U.S.C. **102(e)** as being anticipated by US Patent 5,969,108 (McCafferty et al) (filing date Jan 1993) ((hereinafter referred to as the **'108 patent**). The previous rejection is maintained for the reasons of record as set forth in the previous Office actions.

Discussion and Answer to Argument

7. Applicant's arguments have been fully considered but they are not persuasive for the following reasons (in addition to reasons of record). Each point of applicant's traversal is addressed below (applicant's arguments are in italic):

Applicants argue that the reference does not specifically teach the following elements:

A.) "vector unique restriction enzyme cleavage site".

B.) "first and second cloning region".

C.) "a member of a first plurality of polynucleotides and a member of a second plurality of polynucleotides". (Reply, pp. 6-11),

For Element A: "vector unique restriction enzyme cleavage site".

First, the instant claims (Claim 1 and 11) do not recite exactly the phrase, "vector unique restriction enzyme cleavage site". Applicant is respectively directed to the rejection under 35 U.S.C. 112, 2nd paragraph for further discussion of the claim language.

In support of applicant's argument that the '108 patent does not teach element A.), applicants states "the '108 patent teaches that "It would be useful to design vectors that enable the use of restriction enzymes that cut DNA infrequently" (col. 41, lines 62-63; emphasis added)." First, the said quoted statement is NOT found at "col. 41, lines 62-63" in the '108 patent. Second, it is not clear how the above cited statement by applicant indicates that '108 patent does not teach element A.). However, even without knowing the context from which the above said quotation is extracted, the said quotation on its face value would suggest unique restriction sites in a given vector because the term "infrequently" would suggest uniqueness.

Indeed, it is known in the art that unique restriction sites are standard features in the cloning regions (or multiple cloning sites (MCS)) of a given cloning or expression vector, because this would lead to successful cloning of inserts without destroying the integrity of the vector itself (see "Cloning Vector" and "MCS" downloaded from Wikipedia; downloaded 3/3/07). Without unique restriction sites that only cut within the cloning sites, the vector would be cut into pieces and would not serve the purpose of cloning inserts. In other words, vectors comprising various inserts CANNOT be generated without unique restriction sites within the cloning regions. Thus, to argue the '108 patent does not teach "unique restriction sites" is similar

in arguing that the patent is not "enabled" for creating vectors comprising various inserts. However, applicant has not provided evidence to indicate that the various vectors comprising various antibody inserts, as taught by the '108 patent, are not successfully made.

Contrary to applicant's assertion, the '108 patent have demonstrated various cloning vectors having unique cloning restriction sites. For example, the '108 patent describes using "fd-DOG1" vector (col. 88, lines 62+; Example 39), which was digested (or cut) with restriction enzymes PstI and XhoI for cloning an insert. Thus, the restriction sites for PstI and XhoI are "vector unique restriction enzyme cleavage sites", as defined by the instant specification (pp. 5-6, bridging para).

For element B: *"first and second cloning region"*.

Applicants also argue that the '108 reference does not teach element B.), and the reference only teach "a single cloning site" (emphasis provided by applicant; Reply, p. 8, para 2). First, the terms first and second cloning regions are not specifically defined in the instant specification. Thus, any region that has unique restriction sites and allow for insertion of a polynucleotide of interest would constitute a "cloning site". As discussed above, the '108 patent teaches various vectors that comprise various "cloning sites". For example, the "fd-DOG1" vector (col. 88, lines 62+; Example 39) has at least two unique restriction sites, PstI and XhoI, in the cloning sites of the vector. Thus, the region that comprise the PstI site would be consider as one cloning region, and the region that comprise the XhoI site would be considered as another cloning region. In other words, the vector, "fd-DOG1", has a first and a second "cloning site", as required by the instant claims.

Applicants also argue that the reference only teaches insertion of "one continuous fragment", which "is then inserted into a single site in a vector". (Reply, p. 8, para 2). As discussed above, the cloning site of the vectors taught by the reference reads on the "first and second cloning regions" of the instant claims. Applicant's argument regarding the "one continuous fragment" is also not persuasive, because the said phrase is pertaining to how the polynucleotide is made. Regardless how the VH and VL fragments (whether as one single piece or two separate pieces) were inserted into the vector, the structure of the end product is the same. In other words, the "polynucleotide(s)" resulted from inserting "one continuous fragment" into a cloning vector", as taught by the '108 patent, is structurally the same as the "polynucleotide(s)" claimed in the instant application.

For element C: *"a member of a first plurality of polynucleotides and a member of a second plurality of polynucleotides".*

Contrary to applicant's assertion, the '108 patent teaches element C, as discussed in the previous Office action and is quoted below:

"The reference ('108 patent) does specifically teach a library of vectors comprising both various heavy chain variable regions (a first plurality) and various light chain variable regions (a second plurality). For example, the reference teaches a vector comprising at least two cloning sites comprising restriction sites, ribosome binding site (RBS), and the antibody variable regions (reading a the first and second plurality) (see Figure 45). Although Figure 45 depicts a vector with one particular heavy and one particular light chain variable region, such a vector can be used to generate a library of vectors that comprises different heavy and light chain variable regions. Indeed, the reference teaches the generation of such a library of vectors in detail (see Examples 26 and 39). For example, Example 39 teaches the following (see col. 88, lines 44+):

> "This example shows that functional Fv fragments can be expressed on the surface of bacteriophage by non-covalent association of VH and VL domains. The VH domain is expressed as a gene III fusion and the VL domain as a soluble polypeptide. Thus Fv fragments can be used for all the strategies discussed for Fab fragments including dual combinatorial libraries (example 26)."

In other words, the reference teaches the vector depicted in Figure 45 (corresponding to Example 39) can be used to express both the variable heavy chain domains (the first plurality) and variable light chain domains (the second plurality) to form library of antibody fragments via non-covalent association. Specifically, the reference teaches the vector depicted in Figure 45 can be used to generate dual combinatorial libraries (see col. 88, lines 48+), i.e. a vector library comprising two pluralities of variable regions.

Example 26 (as alluded to in Example 39) of the reference provides additional teachings of generating a library of vectors that encode different heavy and light chain variable regions. Specifically, Example 26 recites the heavy and light chains of antibody fragments can be encoded together in the same vector or in different vectors (see col. 68, lines 22+). Furthermore, Example 26 teaches the generation of antibody libraries with different heavy and light chain variable regions with both the heavy and light chains encoded by the same vector (see bridging para. of Cols. 68 and 69). In addition, Example 26 teaches that the libraries of heavy and light chains (reads on the first and second pluralities) can be expressed from the same vector using different promoters as separate transcripts (see col. 69, lines 7+), hence separate translations that require separate ribosome binding sites on the same vector."

Applicant traversed the above discussion of the reference's teaching by stating the following:

Applicant states Figure 45 does not "depict a vector that comprise two cloning regions into which two polynucleotides are cloned" because the Figure only "shows a map of the insert of sequences" (emphasis provided by applicant; Reply, p. 9, para 3). Applicant also argues that the "one insert can be inserted into one cloning region of a vector". (Reply, p. 9, para 3).

However, the instant claims (Claim 1 and 11) are not claiming the empty vector (i.e. the cloning vector without the antibody (VH and VL) inserts) *per se*. The instant claims recite a plurality of polynucleotides or "vector" comprising "inserts". The relevant question here is to compare the structure of the cloned vectors (i.e. the vectors with the inserts) of the reference's teaching with the structure recited in the instant claims. It would be improper to compare the structure of an empty vector as taught by the reference with the structure recited in the instant claims.

The "insert" depicted in Figure 45 is part of the vector (or polynucleotide) comprising the said insert" as stated in Example 39 (e.g. col. 89, lines 5+) of the reference.

Further, applicant's argument regarding inserting "one insert" into "one cloning region" is also not persuasive. As discussed above under "element B", each of the two unique restriction sites that were used for cloning the insert can be viewed as one cloning region. Thus, the two restriction sites satisfy the two cloning sites requirement as recited in the instant claims. In addition, applicant's statements regarding how the end product (the cloned vector comprising the insert of VH and VL chains) is generated (whether inserting in one cloning region or two cloning region; Reply, p. 10, para 2+) is arguing for the process from which the product is made. Applicant's have not demonstrate how the end product of the vectors containing both the VH and VL regions taught by the '108 patent are structurally different from the claimed product of the instant application.

It is also noted that besides Examples 26 and 39, Example 14 of the reference also recites a plurality of polynucleotides that comprise both various VH (the first plurality of polynucleotides) and various VL (the second plurality of polynucleotides) domains as well as the other required elements in the vectors, such as the ones described in Examples 3 and 5.

Applicant also seems to argue that "Example 39"alone and "Example 26" alone does not teach two pluralities within the generated library of polynucleotides (or vectors). (Reply, pp. 10-11).

However, the reference's teaching needs to be considered as a whole. As recited above, the specific teaching of the Examples of the '108 patent was discussed together.

As discussed in the previous Office action and above, Example 39 of the reference teaches vectors comprising both VH (first variable polynucleotide) and VL (second variable polynucleotide), 5' flanking RBS, 2 cloning sites, unique restriction sites, etc. Example 39 further teaches that the vectors are used for generating "dual combinatorial libraries" (i.e. a plurality of VH with a plurality of VL regions) as described in Example 26. Thus, the reference teaches all the structural requirements for the instantly claimed "a plurality of polynucleotides" or "vectors".

Applicant also argues that the Examples cited above only teach inserting the variable regions (VH and VL) as one single piece of PCR product, and not inserted as two pieces of polynucleotides. However, regardless how the insertion is made (whether as one piece or two piece), the two variable regions (or two polynucleotides encoding for VH and VL) are inserted into the vector at each of the two "cloning regions" (the two restriction sites). In addition, the insertion by "two separate fragments" is not a feature recited in the instant claims.

Therefore, the reference ('108 patent) teaches every elements of the present invention, and anticipates the present invention of a library of vectors comprising two cloning sites, which comprises two repertoires of different variable polynucleotides.

Rejection over '306 Patent

8. Claims 1-3, 11-12, 15-16 are rejected under 35 U.S.C. **102(a)** as being anticipated by EP 844306 A1 (hereinafter referred to as the **'306 patent**). The previous rejection is maintained for the reasons of record advanced on page 3 of the office action mailed on 12/29/2005.

Discussion and Answer to Argument

9. Applicant's arguments have been fully considered but they are not persuasive for the following reasons (in addition to reasons of record). Each point of applicant's traversal is addressed below (applicant's arguments are in italic):

Applicants traversed the above rejection with the same argument as the traversal over the '108 patent. Thus, applicants are respectively directed to the discussion under the '108 patent for answer to arguments.

Rejection over '197 Patent

10. Claims 1-3, 11-16 are rejected under 35 U.S.C. 102(e) as being anticipated by US Patent 6,172,197 B1 (McCafferty et al) (hereinafter referred to as the **'197 patent**). The previous rejection is maintained for the reasons of record advanced on page 6 of the office action mailed on 12/29/2005.

Discussion and Answer to Argument

11. Applicant's arguments have been fully considered but they are not persuasive for the following reasons (in addition to reasons of record). Each point of applicant's traversal is addressed below (applicant's arguments are in italic):

Applicants traversed the above rejection with the same argument as the traversal over the '108 patent. Thus, applicants are respectively directed to the discussion under the '108 patent for answer to arguments.

Claim Rejections - 35 USC § 103

12. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

13. Claims 1-3, 11-12, 15-16 are rejected under 35 U.S.C. 103(a) as being obvious over either US Patent 5,969,108 or US Patent 6,172,197. The previous rejection is maintained for the reasons of record advanced on page 8 of the office action mailed on 12/29/2005.

Discussion and Answer to Argument

14. Applicant's arguments have been fully considered but they are not persuasive for the following reasons (in addition to reasons of record). Each point of applicant's traversal is addressed below (applicant's arguments are in italic):

Applicants argue that "no reasonable expectation of success has been articulated by the Office Action"(Reply, p. 12, para 2).

Although the term "reasonable expectation of success" was not explicitly used in the previous office action (mailed 12/29/05), the discussion under the 103(a) rejection demonstrates "reasonable expectation of success". As discussed in the previous Office action (p. 8+), the '108 or the '197 patent teaches various vectors and methods of inserting various antibodies variable regions into the vectors. Thus, it is has been demonstrated that various vectors with various desired antibody variable regions (such as a combination of both VH and VL regions) can be successfully inserted into a cloning vector, and generate a plurality of polynucleotides comprising the inserts.

Applicants also argue the proposed modification would render the prior art unsatisfactory for its intended use (Reply, p. 13).

Applicant has not demonstrated how the modification would render the prior art unsatisfactory for its intended purpose. It is not clear how "two fragments" would not be satisfactory for cloning into a single cloning region in a vector. In other words, applicant has not demonstrated the two fragments would not be cloned into a cloning region. Most importantly, applicant has not demonstrated how the modification would not produce a product with the same or substantial similar features as the claimed product.

Applicants also argue "the proposed modification would change the principle of operation of the cited references".

Again, applicants are arguing the differences of the methods for generating the final products between the references' teachings and the claimed invention. However, the question here is whether the end product (i.e. the claimed polynucleotide) would be redesigned, not whether to redesign the process for making the products.

New Rejections

Claim Rejections - 35 USC § 112

15. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

16. Claims 1-3, 11, 12, 15 and 16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recite "complete antibody constant region or a part of an antibody variable region ..." (emphasis) in lines 16 and 25 of the claim. It is not clear if the recitation following the term "or" is part of the claimed Markush group, or the recitation is modifying the species immediately preceding the term "or". The term "and" is usually used for a proper Markush claim construction. (see MPEP 803.02).

Where applicant acts as his or her own lexicographer to specifically define a term of a claim contrary to its ordinary meaning, the written description must clearly redefine the claim term and set forth the uncommon definition so as to put one reasonably skilled in the art on notice that the applicant intended to so redefine that claim term. *Process Control Corp. v.*

HydReclaim Corp., 190 F.3d 1350, 1357, 52 USPQ2d 1029, 1033 (Fed. Cir. 1999). The term "encodes" in lines 12 and 21 of Claim 1, and lines 12 and 21 of Claim 11 is used by the claim to mean "comprise", while the accepted meaning is for a polynucleotide to encode for a polypeptide, as it is used in elsewhere of the said claims. The term is indefinite because the specification does not clearly redefine the term.

Claims 1 and 11 recite the phrase "for the vector unique, restriction enzyme cleavage site", which is unclear. It is not clear if the phrase is referring to a "unique vector", or a "unique restriction enzyme cleavage site".

Claims 1, 15 and 16 recite the term "Fab", however, the said claims also recite that the "polypeptide" is "a complete antibody variable region". Applicant's usage of the term "Fab" to refer to only an antibody variable region is "repugnant" to its ordinary meaning in the art. It is also conflicting with the usage of the term "Fab" in the instant specification, where, for example, "Fab" is referring to fragments "consisting of VL, VH, CL and CH1 antibody domains" (p. 14, lines 22+ of the spec.). Thus, the claim is rendered indefinite because a person of ordinary skill in the art would not be able to define the metes and bounds of the instant claimed invention.

Claim Rejections - 35 USC § 102

17. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim Rejections - 35 USC § 103

18. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

(Note: the instant claim numbers are in bold font.)

19. Claims 1-3, 11, 12, 15 and 16 are rejected under **35 U.S.C. 102(b)** as anticipated by or, in the alternative, under **35 U.S.C. 103(a)** as obvious over McCafferty et al (WO92/01047; 1/23/92; PCT publication of the 5,969,108 patent). *It is noted that the content of the cited reference is substantially the same as the previously cited '108 patent.*

The instant claims recite "A plurality of polynucleotide encoding a Fab library, the library comprising a plurality of vectors wherein each vector of the plurality of vectors comprises:

- a first cloning region and a second cloning region ...
- a polynucleotide encoding an anchor region ...
- a member of a first plurality of variable polypeptides ...
- a member of a second plurality of variable polynucleotides ...
- a polynucleotide encoding a tag ..."

(see instant claims 1 and 11).

McCafferty et al, throughout the publication, teach various libraries of polynucleotides comprising various antibody domains.

The reference teaches various polynucleotides comprising various antibodies or fragments thereof (see Examples 1-48).

The reference teaches vectors comprising the followings (See Figures 5 and 45; Examples 14, 26, 39),:

A). Restriction sites for cloning such as the PstI and XhoI sites of the "fd-DOG1" vector (Example 39; p. 109, lines 44+), which reads on the first and second cloning regions of **clms 1 and 11**. The PstI and XhoI restriction sites read on the "vector unique, restriction enzyme cleavage sites" of **clms 1 and 11**. The reference also teaches "pelB" and "geneIII leader sequence" that are 5' to the cloning sites in the vectors (Figure 45), which read on the signal sequences of **clms 1 and 11**. The reference also teaches "ribosomal binding site" or (RBS) 5' to the cloning sites, which reads on the RBS of **clms 1 and 11**.

The reference also teaches various anchor regions such as "gene III" that is 3' to the cloning regions, which reads on the anchor regions of **clms 1 and 11**.

The reference also teaches inserting various polynucleotides encoding for antibody variable regions such VH and VL, as well as the antibody constant regions (CH and CL) into the vectors to generate various libraries (See Figures 5 and 45; Examples 14, 26, 39), which the polynucleotides read on "a first plurality of variable polynucleotides" and "a second plurality of variable polynucleotides" of **clms 1 and 11**. The various variable regions (VH and VL) and the constant regions also read on the VL and VH of **clms 2 and 12**.

The reference also teaches using the taught techniques to generate libraries with various sizes such as 10^{14} (p. 8+), which reads on the library sizes recited in **clms 3, 15 and 16**.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sue Liu whose telephone number is 571-272-5539. The examiner can normally be reached on M-F 9am-3pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Doug Schultz can be reached at 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

JON EPPERSON
PRIMARY EXAMINER

SL
Art Unit 1639
3/2/2007